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Report

Readiness of food composition databases and food component analysis systems for nutrigenomics

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ABSTRACT

The two-fold purpose of this paper is to examine the adequacy of food composition databases and dietary assessment techniques to meet the needs of nutritional genomic research and to explore the challenges and opportunities presented by the emerging field of nutrigenomics to future development of food composition databases and food composition analysis systems. A review of published literature and the Internet for organizations and their ongoing dialogues were used to explore how current food composition databases and nutritional assessment methodology could be made more useful in nutrigenomics research. An outline of current projects and potential approaches to develop more reliable and cost-effective methods for the study of nutrigenomics in diverse populations is presented. Many issues related to these dietary and database methodologies need to be addressed and overcome if nutrigenomics is to reach its potential for promoting optimal health through better individualization of diet and physical activity recommendations. To meet the complex research and clinical challenges of individualizing nutrition and health care, a network of diverse health care professionals and scientists is needed to move the world toward optimal health practices.

1. Introduction

A recent headline of the American Public Health Association Newsletter heralded genomics as a new tool for improving public health but noted a host of hurdles must be overcome before it can be fully integrated into public health practice (Johnson, 2008). Nine of the top 10 leading causes of death, especially chronic diseases such as heart disease, diabetes, and cancer have important genetic components that interact with modifiable environmental factors including diet and physical activity (CDC, 2008a). Some maintain this is the dawning of the era of personalized medicine and nutrition (Allison, 2008).

With the publication of the Dietary Reference Intakes between 1997 and 2005, the emphasis in the field of nutrition moved from preventing nutrient deficiencies toward a goal of optimal nutrition (Otten et al., 2006). The Recommended Dietary Allowances (RDAs) were expanded from the single RDA value to four reference values. The 2005 revision of the USDA MyPyramid Food Guidance System (USDA, 2008a) changed guidelines to provide a range of intakes according to additional factors such as gender, age, body mass index, and activity levels. The growing awareness that one size does not fit all and the success of the Human Genome Project (HGP) between 2001 and 2003 brought into focus the importance of genes in defining optimal nutrition (Horowitz, 2005). HGP goals included identifying, mapping, and sequencing of all the genes in human deoxyribonucleic acid (DNA); storing the data in a database; improving tools for data analysis; and addressing ethical, legal, and social issues (HGP, 2008). A new specialized area of nutrition today called nutrigenomics began to take shape that would attempt to study and incorporate the scientific and technological advances into dietetic practice (Ommen and Groten, 2004; Rosen et al., 2006; Trujillo et al., 2006). The two-fold purpose of this paper is to evaluate what is needed by researchers to develop nutrigenomics as the basis for individualized health promotion and chronic disease prevention in humans and to summarize the challenges human nutrigenomics presents to existing food composition databases and food composition analysis systems.

2. Definitions

Nutrigenomics, sometimes termed, nutritional genomics, describes the biological and statistical interaction among dietary

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chemicals and genetic make-up. These interactions vary because individuals have unique combinations of common gene variants that are differentially affected by diet (Kaput and Rodriguez, 2004). The relationship between diet and genes impacts the effects of diet on disease risk susceptibility, nutrient requirements, and even treatment modalities (Gillies, 2003; Ontovas and Corella, 2004; Trujillo et al., 2006; Stover and Caudill, 2008). This new genetic nutrition approach describes nutrients in one of their biological roles, that is, as "signaling molecules" that are recognized by cellular sensing mechanisms and result in translation of these dietary signals into changes in gene, protein, and metabolite expression (Afman and Muller, 2006). At the genomic level, Afman and Muller (2006) state that these molecular changes serve as dietary "signatures" or fingerprints that can precisely annotate the phenotype, particularly under conditions of metabolic stress and early phases of organ-specific changes, e.g. insulin resistance.

3. Nutrigenomic goals, challenges and outcomes

The goals and expected outcomes of nutrigenomics are to: (1) prevent or delay onset of disease and optimize or maintain human health (Kaput and Rodriguez, 2004; Trujillo et al., 2006); (2) identify individuals who are responders and can benefit from specific dietary interventions (De Busk et al., 2005; Davis and Milner, 2007); (3) develop evidence-based healthful food and lifestyle advice and dietary interventions (Afman and Muller, 2006); (4) identify how human genetic variation affects nutritional requirements (Stover, 2006; Stover and Caudill, 2008); and (5) expand understanding of genetic mechanisms underlying health, the basis of individual variation, and conditions when diet influences metabolism (Stover, 2004). The goal of "individualizing" or "personalizing" nutrition for a single unique individual may or may not be achievable and some have questioned whether it is desirable based on social and cultural issues (Penders et al., 2007). Realistically, focusing on subgroups of people who share certain common genetic traits may be more practical and effective (Kaput, 2008). This process of identifying subgroups within a population who share common genetic traits is often termed placing individuals into a bin and is similar to dividing individuals into quintiles. See Fig. 1 for a graphic illustration of subgrouping individuals by a genetic trait. Current nutritional, genetic, and biomedical knowledge, however, is based largely on animal or large population studies that may or may not be applicable to individuals within these populations (Kaput, 2008). Creating individual recommendations for nutrition will be a significant challenge.

4. Commercialization of nutrigenomics

As the nutrigenomics field progresses, areas of commercialization are emerging such as companies offering diets designed for individuals based on genetic analyses of between one and about thirty gene variants; more than 500 tests of genetic variations exist (Bowen et al., 2005). A nonprofit think tank has referred to this activity as "patenting and profiteering" (GeneWatch, 2006). Researchers indicate that the current scientific evidence is not sufficient to recommend using genetic profiling when developing diet and lifestyle recommendations for optimal health or disease prevention (Cecile et al., 2008; Hudson et al., 2007; Janssens et al., 2008). The American Society of Human Genetics position is that direct-to-consumer genetic testing presents several potential risks to consumers related to laboratory quality, assay validity, false or misleading claims, and lack of counseling to interpret and apply test results (Hudson et al., 2007). Another area of commercialization is the growing interest in the development of functional foods that can be marketed to consumers (Roodenburg and Leenen, 2007). The global market for fortified and functional foods is projected to grow by at least 7% each year (Sloan, 2002; Subbiah, 2006), and this growth rate will signal the need for more food component analysis of foods and expansion of existing food composition databases (Hudson et al., 2007).

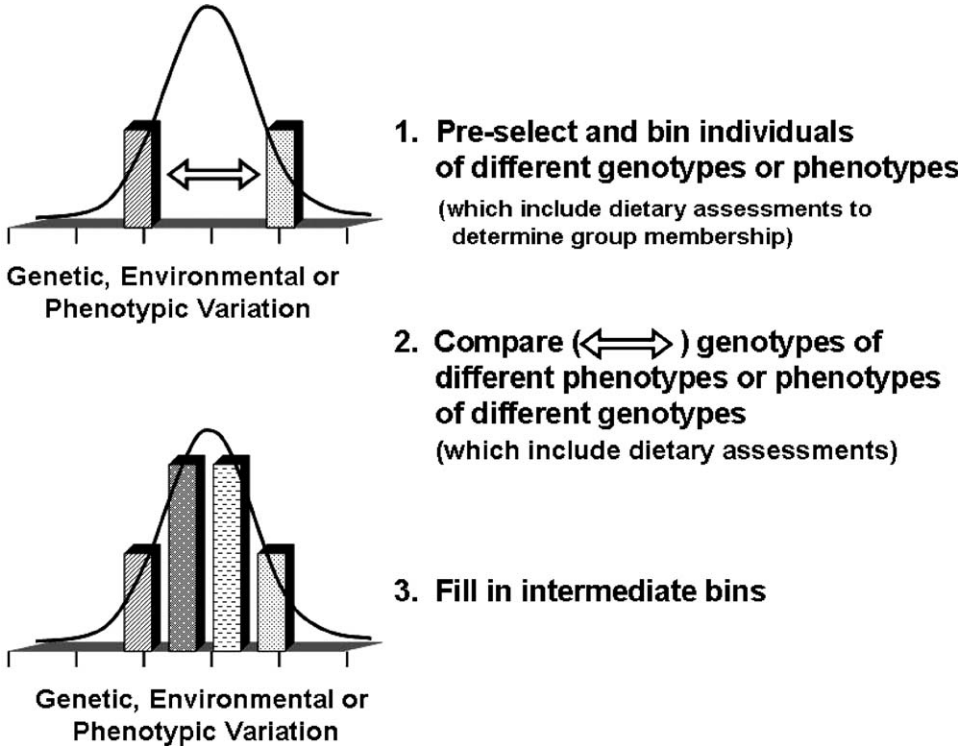

Fig. 1. Strategy for identifying metabolic subgroups.

5. Challenges and opportunities in nutrigenomics research

As research and technology advances, so will progress toward personalized nutrition in the future. Some consumers and some commercial firms appear anxious to pursue the advantages promised by nutrigenomics now, regardless of inadequate scientific knowledge. While clinical trials are considered the strongest evidence for clinical applications, these types of studies will be difficult to plan and conduct without further development of tools and techniques, especially related to databases and dietary assessment methodologies (Fogg-Johnson and Kaput, 2007; Kaput et al., 2006). The need for more food analyses, specifically of the bioactive substances not traditionally considered nutrients, is increased (Fogg-Johnson and Kaput, 2007). A full food component profile cost about 2000 US dollars per sample in 2002 (Haytowitz et al., 2002). An international ranking scheme will likely be needed to prioritize analyses of foods, and many developing countries will not have the resources for analyzing their local foods.

A further challenge is the need for harmonization of food composition databases (Slimani et al., 2007b). While harmonization of databases is usually thought of as the use of common units by two or more databases, the term standardization may also apply, e.g. international system of units in which an international group of scientists have designated seven units as the standard unit for scientific studies. This means that mathematical formulas may be used to translate from one unit to another. The question is whether modern computers might allow even more complex translation in food composition research. Food and food component intake data are gathered by a variety of dietary assessment tools and entered into food component analysis programs that produce output in food composition and food component units, e.g. water (g), energy (kcal or kJ), macronutrients (g), etc. These outputs can be in common units, but the results are not considered to be comparable between differing dietary tools. Ideally, statistical methods might be developed by which adjustments could be made that might allow data collected by one tool to be harmonized with data collected by another tool. These methods are not available at this point and future instruments may be developed that negate the need for such methods. The other harmonization needed would be the "back translation" of food components into foods. If nutrigenomics can identify the likely level of one or more nutrients or food constituents needed for a metabolomic reaction, a need then exists for a database by which these levels can be converted into specific foods.

Harmonization and standardization would allow databases from various countries to be brought together into a universal database and potentially could assist in global study of nutrigenomics (Charrondiere et al., 2002). A start has been made in the European Prospective Investigator of Cancer and Nutrition (EPIC) collaboration of ten countries to develop a standardized food composition database, European Nutrient Database (ENDB), to allow comparability of nutritional studies across countries (Slimani et al., 2007a). While not new to food composition databases, the need for harmonization becomes greater for nutrigenomics research to be conducted on a global scale (Charrondiere et al., 2002).

The most complete set of food composition data in the US is the USDA National Nutrient Database for Standard Reference (USDA, 2008c), and the European Union has developed the comparable European Food Information Resource Network EuroFir database (EFIRN, 2008). Environmental conditions under which organisms develop may modify growth and genotype. For example, Reynolds et al. (2005) note that plant species, like other organisms, respond to their environments, which may result in different food component contents depending on the genotype of the plant and its growth conditions. The Food and Agriculture Organization of the United Nations and various national governments have developed food composition tables for many countries worldwide but data must often be extracted from unlinked flat files or print publications and some are based on extrapolations from databases in Western Countries (INFOODS, 2008a). Nevertheless, progress in developing national and international food composition databases is being made, as noted by the International Life Sciences Institute Crop Composition Database (2006), the International Network of Food Data Systems (INFOODS, 2008b,c), the aforementioned EuroFir database and the ENDB project (Slimani et al., 2007b).

6. Influences on diet and gene interaction assessments

An added layer of complexity occurs when comparing food and food component intakes across populations. Cultural differences in food manufacturing, preparation, and eating customs exist not only among nations and ethnic groups but also among religions (Kim and Sobal, 2004). Personal choices such as various vegetarian practices, sleep time quality, activity levels, and other factors (Kaput et al., 2005) will also confound assessments of food component intakes. Individual studies have successfully included one or more of these choices or habits, but no study has been published with most of these environmental factors incorporated (Bell and Tepper, 2006; Ma et al., 1997). Knowledge of variance in food composition for given foods and given varieties of selected foods will be critical to the development of databases that can estimate or assess consumption sufficient for the study of nutrigenomics in humans (Stover and Caudill, 2008).

7. Dietary assessment for nutrigenomics

While dietary intake is considered a critical environmental exposure affecting the relationships of many genetic factors and disease risks, the complexity and variance in dietary intake has limited the attention paid to nutrition by many geneticists (Kaput and Rodriguez, 2004; Kaput et al., 2005). Biochemists who focus on carefully controlled animal studies view self-reported dietary data by humans as having questionable reliability. Epidemiologists who analyze dietary patterns in large population studies view many of the dietary methodologies as too burdensome, too expensive or too labor intensive. Advanced statistical methods with structured equations may prove helpful in assessing intakes (Dodd, 2006; Dwyer et al., 2003; Tooze et al., 2006). The application of statistical methods to estimate usual intake, such as that proposed by Guenther et al. (1997), can be helpful if there are sufficient data available on food intake variation in the population of interest. Subar et al. (2006) have proposed a food propensity questionnaire analysis as a new approach by quantifying a relationship between frequency responses and a 24 h recall that might be used effectively as covariates in statistical models to better estimate usual intake of less regularly consumed foods. The science of nutrigenomics has not yet addressed the level of precision needed to analyze food component–gene interactions that alter physiological processes.

Many recent nutrition studies have focused on large free-living populations rather than on individuals in controlled environments such as metabolic wards (Slimani et al., 2007a,b). These studies necessitated the development of dietary assessment methodologies that could be used effectively with free-living populations. The majority of American epidemiological studies have used a food frequency questionnaire (FFQ) as the method of choice due to ease, time, cost, and ability to retrieve dietary consumption over time. The National Health and Nutrition Examination Survey (NHANES), a large national study, collects a 24 h dietary recall in person and a second 24 h recall via telephone (CDC, 2008b). The food record is another method to assess usual food intake, but the proposed

number of days of records required to establish confidence in usual intake of different food components varies considerably depending on age and gender and whether group means or individual means are desired. For example, 3 days of food records are needed to estimate energy intake for male group data compared with 27 days of food records for individual male data (Basiotis et al., 1987). For vitamin A intake, 39 days of food records are needed to estimate means for male group data compared with 474 days for individual males (Basiotis et al., 1987).

Tucker (2007) provides a succinct summary of the advantages and disadvantages of common dietary assessment methods used in large population studies and concludes that the FFQ remains the most cost-effective tool for usual food intake in large populations. Yet individualized nutrition studies will likely need to assess subgroups of populations with given phenotypes and both similar and dissimilar food exposure (Kaput, 2008). In examining diverse populations or diverse subgroups within a population, the assessment methods and databases needed to study these diverse groups within feasible timeframes, costs, and respondent burden have not been adequately addressed. A potential solution is to first analyze specific food data by existing food composition software and then to enter these analyzed values of nutrients and bioactive components into an internationally harmonized database developed to allow comparison of nutrient and bioactive components among studies regardless of the dietary assessment method used to collect the specific food data (Kaput, 2007, 2008). Eventually, another database would need to be developed to convert nutrient and bioactive components back into a food-based database to translate the information into counseling for clients.

Because individual researchers may have preferences for dietary assessment tools such as FFQs, food records, or 24 h recalls, each study generates independent and unlinked databases. Dietary analysis software is usually designed for either the 24 h recall or food record type of assessment while FFQs have unique assessment programs with weighed food component values based on the population or subpopulation for which the FFQ is designed. The result of these practices is that sharing or comparing food component intake data among studies is cumbersome and time-consuming. An urgent and pressing need, therefore, is the development of a relational database capable of capturing food component intake from a variety of assessment methods and converting food consumption into chemical analyses based on accepted food composition databases. This type of database would be analogous to the ever-expanding biomedical research databases that are capturing molecular, genetic, proteomic, clinical, and metabolomic data from human studies. A significant challenge for such databases would be to account for cultural differences in food manufacturing, preparation, and eating that includes religious customs.

Linking dietary intake assessment databases to metabolomic and genomic data will eventually lead to the ability to more accurately monitor food intake through analyses of serum or urine metabolite concentrations.

8. Potential approaches for nutrigenomic research

Given the promise of health benefits from individualized nutrition, the detailed studies needed to expand our knowledge base must be carried out in a reasonable and economically feasible manner. One possible plan is to establish dietary patterns and genetic patterns of health and disease within subgroups of the population. Obtaining research data on dietary patterns and genetic patterns, especially among minority and rural populations who have not been involved in the large national surveys and who lack knowledge of or trust in medical research is (i.e. individuals without experience in prior research or in even receiving medical care on a regular basis) presents special challenges (McCabe-Sellers et al., 2008). An emerging research method for translational research in health disparities is the community-based participatory research (CBPR) approach used by the Delta Nutrition Intervention Research Initiative (Ndirangu et al., 2007, 2008; Zoellner et al., 2007). The CBPR approach involves establishing an ongoing presence and trust between community residents and researchers that educate residents about the value, benefits, and principles of human research and, thereby, develops an equitable partnership in planning, designing, implementing and evaluating research studies based upon the community's health priorities (Chen et al., 2006; Ndirangu et al., 2007; McCabe-Sellers et al., 2008).

9. Collaborations in communities

Collaboration across local, state, and regional agencies and institutions and across many disciplines begins with dialogues in which community residents are seen as having expertise and valuable knowledge to bring to the research planning as well as recognizing that community residents can be trained to be knowledgeable and skillful in Institutional Review Board principles, data collection techniques, recruitment, retention, and especially interpretation of data when analyzed. Some examples of these types of collaboration include those from the Mississippi Delta (Ndirangu et al., 2007, 2008; Yadrick et al., 2001; Zoellner et al., 2007) and from Virginia (Chen et al., 2006). Dialogues can begin collaboration with innovative steps to secure knowledge of the benefits that genetic research can bring to individuals and to their communities (McCabe-Sellers et al., 2008).

10. New technology applications

Another possible approach is to apply more technology to dietary data collection and data entry about diets and foods. Bar coding is one technique that holds promise of scanning specific foods in household inventories; however, some grocery firms consider bar coding as proprietary data. The US bar code system contributes to the development of point-of-purchase dietary assessments because each manufacturer is provided a 3-number code identifying the company, but each product number is generated within the company. The Food Marketing Institute (2007) reports that the average US supermarket carries about 45,000 items. Although not all items are food, the number of different manufacturers and, therefore, unknown bar code–food component profiles is large and difficult to monitor.

The Internet holds future promise for self-administration of FFQs and for self-assessment tools such as MyPyramid Tracker, an online personal assessment (USDA, 2008b). Researchers have used photographs or pictures of food as prompts in dietary interviews, and telephone interviews have extended access to repeated dietary assessment (Martin et al., 2007). Most recently, work has begun using cell phones to photograph and record foods and to assess not only specific foods but also portions of food consumed through new engineering techniques (Boushey, 2009).

Innovative technological methods that improve accuracy in dietary assessment are needed to improve the ability to detect and understand diet–gene relationships. Certainly the advent of newer computer technology and statistical analysis methodology will increase the ability to develop models for closer linkage of various databases.

11. International alliances

Food composition databases have been developed in varying degrees of completeness, largely by global regional database

working groups, and from the expertise of USDA Agricultural Research Service scientists and their counterparts in Canada, the United Kingdom, Europe, and other countries (Baingana, 2004; de Pablo, 2004; Gnagnarella et al., 2004; McBurney et al., 2004; Murphy et al., 2004; van Heerden and Schonfeldt, 2004). Conferences such as the 7th International Food Data Conference held in Sao Paulo, Brazil and the 32nd National Nutrient Databank Conference held in Ottawa, Canada have promoted international networking in the development and maintenance of databases. The large European studies such as the EPIC study about cancer have led to cooperation and collaboration to produce a multi-country food composition database that can serve as a model for a larger international global database (Slimani et al., 2007a,b).

A systems biology approach in which international alliances are formed of diverse disciplines, models, technologies and populations produce a large collaborative network of nutritional genomics researchers with expertise, data, resources and knowledge to harmonize plans and objectives and reduce duplication of efforts (Kaput et al., 2005). This same model could be considered on an international level for dietary assessment methods and databases through alliances formed by diverse researchers from many countries. One such organizational model is the European Nutrigenomics Organization (2008) that provides a continuing Internet dialogue about goals, methods, disciplines, and other issues related to dietary assessment and databases.

While new techniques are being developed and tested, long-term steps need to be taken in other areas. One step is to establish an international dialogue on developing databases and procedures to allow knowledge and best practices to be shared. Some researchers see a need to translate food component data from various dietary assessment methods into one database.

12. Conclusions

The food composition and assessment methodologies and data currently available are not sufficient or adequate to adjust dietary recommendations and develop individualized or "metabolic group" nutrition recommendations due to limited studies outside the north European and North American populations. Even within these populations, individual genetic and dietary variations in many subpopulations have not been well studied. The question that many researchers ask is when will sufficient evidence be available for individualized nutrition and medicine to become a reality. Arab (2004) has said that the availability of information on which to base individualized recommendations depends on the drive and will of the nutritional community, the success in recruiting funding to the area, the education of nutritionists and the spawning of great ideas and approaches.

Dialogue and collaboration among nutritionists, database developers and researchers are needed to develop and harmonize international databases such as ENDB and maintain organizations such as INFOODS that work to improve the quality and quantity of databases to allow nutrigenomics to become a reality. International collaboration and alliances continues across disciplines, institutions, technologies, cultures and borders.

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